A revolutionary leap forward in the well-being of humanity through real-time continuous biomarker and drug monitoring

SPIDEN

# Label-free biomarker sensing

## Leveraging CMOS technology & photonic integration

**Leo Grünstein, Jens Hofrichter, Spiden AG**

**November 15th, 2022**

# Our vision

In the future, our bodies and technology will become one. Continuous health monitoring through next generation wearables and implants will be the standard, allowing us to live longer, healthier lives.

# The problem we solve

Continuous, simultaneous and label-free monitoring of multiple biomarkers and drugs in fluids, cells and tissue presents huge opportunities in pharma and medicine. Adoption, however, has been held back by the complexity and lack of robustness of current technology. We are changing that.

# Our solution

We are a deep-tech start-up, combining a novel optical monitoring platform through integration of unique photonic sensors, light sources and fluidics, with state-of-the-art machine learning methods. This provides superior biochemical specificity and robustness in the most demanding use cases, removing the need for reagents or labels.

# Our goal is to enter the wearables market through launching a Spiden wearable with non-invasive multi-biomarker/drug monitoring capabilities, starting with glucose

SPIDEN

## Wellness oriented glucose monitoring

## Medically oriented glucose monitoring

***Currently available CGM** (continuous glucose monitoring) **devices***







*Cost per year and person, USD/y*

| *1'800* | *2'400* | *2'400* | *2'000* | *3'500* | *4'000* |
|---|---|---|---|---|---|
| *(athlete focused)* | *(diet focused)* | *(diet focused)* | *(revenue: 2.7bn)* | *(revenue: 1.7bn)* | *(revenue: 0.9bn)* |

**All these products are minimally invasive and need to be changed every 1-2 weeks**

***Total addressable market, USD/y***

- Health/diet optimizers: >300bn* (>170m on a diet in US/EU at every given moment, alone)
- Athletes: >7bn* (>4m endurance athletes in US/EU alone)

- Diabetes glucose monitoring: current market at >12bn, of which already 5bn are made up by minimally invasive CGM (continuous glucose monitoring) devices

**USD >300bn in addressable market across wellness and medical**

*And this **is glucose only … imagine a multi-biomarker/drug monitoring device***

**As a reference we take existing continuous glucose offerings which are at roughly USD 2000 per person and year*

# Our learnings of why transcutaneous glucose and multi-biomarker monitoring has not been achieved yet

SPIDEN

**Lack of understanding why it fails**

This is why we follow a stepwise development approach

**See next page**

**Lack of robustness across many people**

This is is why we developed a proprietary integrated computational and measurement strategy to handle the variability

**Lack of specificity and breadth in spectroscopy**

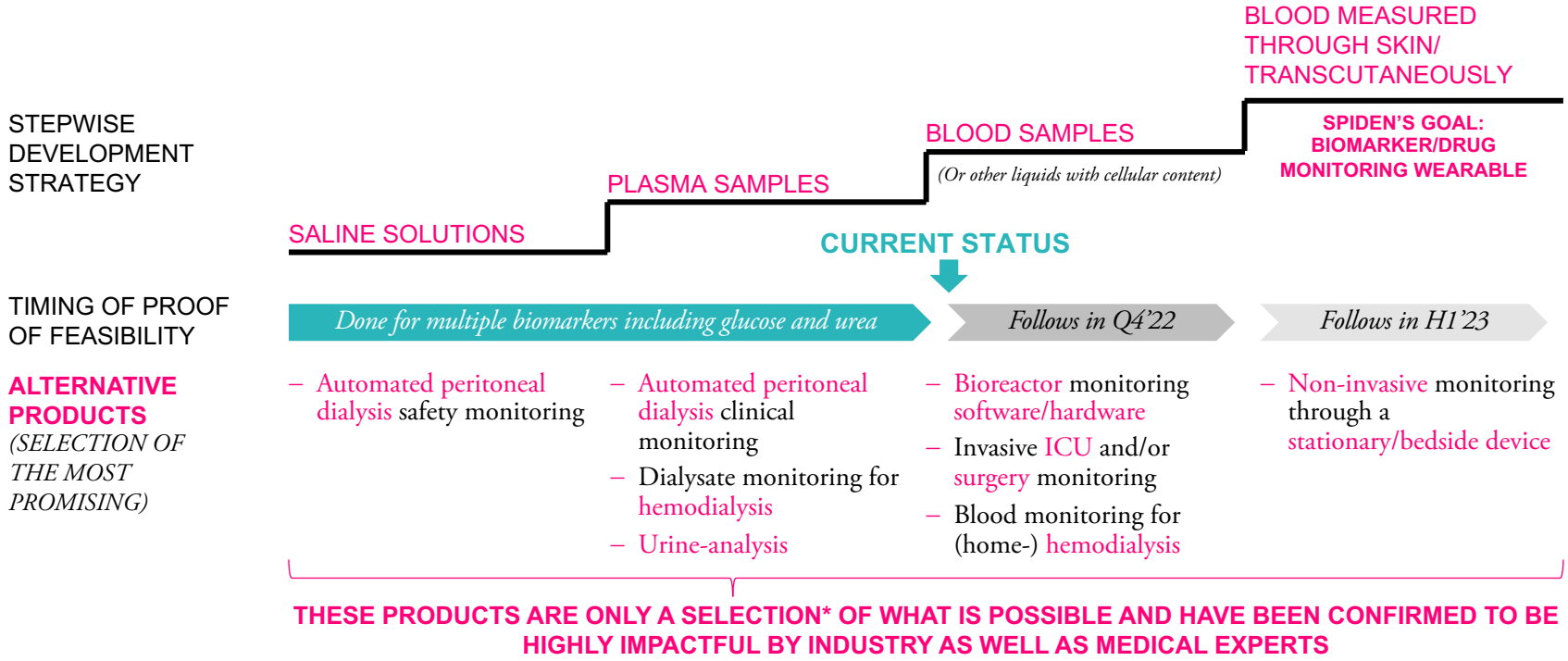
This is why why we believe that using multiple forms of spectroscopy can provide important breadth capturing information necessary for achieving robustness

**Lack of robustness to confounding analytes**

This is why we further develop ML/analytical methods that are able to account for confounding analytes robustly

**We believe that our integrated expertise, infrastructure and approach address these problems**

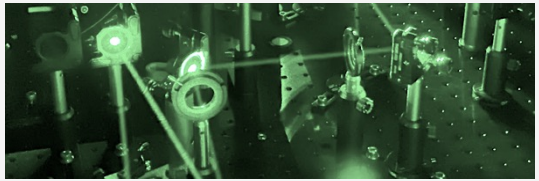
# We follow a stepwise development strategy with the objective to present data proofing our transcutaneous glucose monitoring approach by H1'23



# Spiden built up the critical infrastructure and capabilities to develop these complex assets and products under one roof

**ALL INFRASTRUCTURE IS UNDER ONE ROOF IN A STATE-OF-THE-ART 1800 SQM LABORATORY AND OFFICE SPACE IN PFÄFFIKON (SZ), SWITZERLAND**

## Biophotonics lab

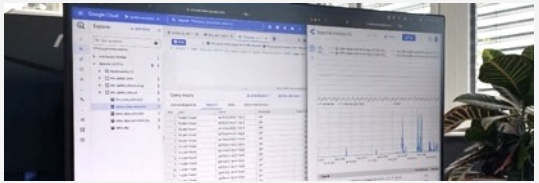


- Multiple highly flexible spectroscopy setups
- Ability to run spectroscopy experiments at scale

## Fluidics lab

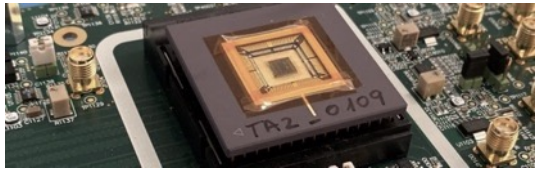
- Methods & equipment enabling design of complex sample/spectroscopy interfaces as well as fluidic systems

## Software & machine-learning infrastructure



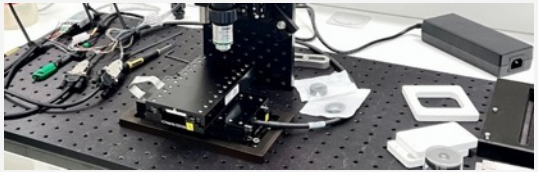
- Integrated pipeline from lab to cloud-based data lake for processing and analysis
- Full-stack capabilities for AI-based products

## Electronics engineering lab



- Proprietary detector chip platform with unique capabilities (high speed, high sensitivity)
- Lab infrastructure for design/characterization

## System engineering lab



- System integration lab with testing capabilities
- Access to applicable standards & regulations

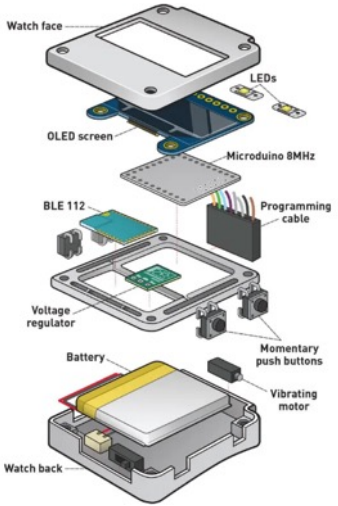
## Biochemistry lab

- Biomedical laboratory on biosafety level 2, with high throughput gold standard testing capabilities
- >100 samples per hour preparation capacity

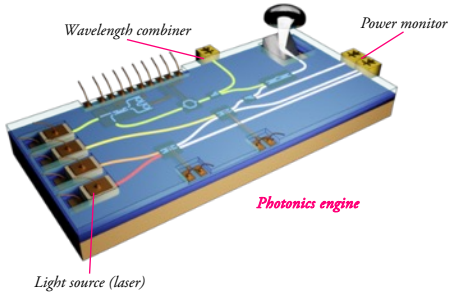
# Focusing on a transcutaneous glucose monitoring wearable, we mainly system-integrate, and only selectively invest in deep tech

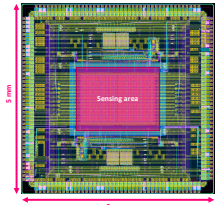
SPIDEN

## A wide range of sophisticated technologies are needed to create a transcutaneous glucose wearable product…




Wearable (example)




Light detector

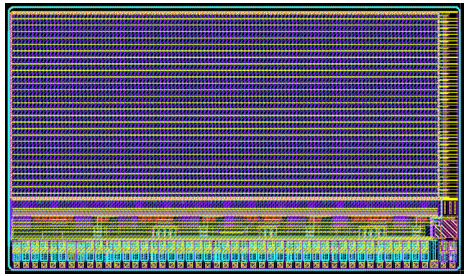
## … and Spiden chooses the most appropriate strategy for fulfilling these needs from a product company perspective

| | Develop | Partner | Source |
|---|---|---|---|
| ML toolchain | | ✕ | ✕ |
| ML algorithms | ✕ | | ✕ |
| Spectral database | ✕ | | ✕ |
| Light sources | | ✕ | ✕ |
| Light guides | | ✕ | ✕ |
| Light detectors | ✕ | ✕ | |
| Photonics engine | ✕ | ✕ | |
| Filters & diffractive elements | | ✕ | ✕ |
| Data processing | | | ✕ |
| Power | | | ✕ |
| Display | | | ✕ |
| Packaging | | | ✕ |

***Spiden created the required inhouse capabilities for system integration and laboratory (incl. data generation/gold standard measurements)***

# Spiden's CMOS detector specification (3rd generation)

## Preliminary datasheet



Spiden's 3rd generation
CMOS detector IC

- Sensor available for 3rd parties
- Contact Spiden for samples

| Characteristics | Value |
|---|---|
| Detector type | CMOS - SPADs |
| Detector manufacturer | Spiden's CMOS foundry partner |
| Cooling | No |
| Key specifications | • Lowest noise<br>• Shortest integration time<br>• Highest sensitivity |
| Applications | • Advanced Raman spectroscopy with fluorescence suppression<br>• Fluorescence lifetime imaging |
| Chip size | 3 mm x 5 mm |
| 3-sides buttable | Yes |
| Pixel array | 232 (c) x 56 (r) |
| Pixel size | 20.3 x 35.8 µm |
| Active SPAD area (diameter) | 9.3 µm |
| Wavelength range | 350 - 950 nm |
| SPAD On/Off | Yes |
| SPADs deadtime | > 15 ns |
| Temporal resolution | > 600 ps gate @ 20 ps steps<br>(one independent gate per pixel) |
| Dark noise | 300 counts/pix/s* |
| Readout noise | 0 |
| Conversion efficiency | >1.5 V / SPAD event |

| Characteristics | Value |
|---|---|
| Imaging mode of operation | • Pixel-by-pixel readout<br>• 1 bit memory per gate per pixel<br>• **Frame rate:** 25.2 kHz (39.7 µs per frame per gate) |
| Spectroscopy mode of operation | • All hit pixels per column are counted<br>• Column-wise readout<br>• 10 bit counter per gate per column<br>• **Frame rate:** 143.7 kHz (6.96 µs per frame per gate)<br>• **Repetition rate:** > 675 ns (inside same frame, per gate)<br>• **Max. repetitions per frame (per gate):** 18 |
| Data rate | 332 Mbps (4 serial outputs @ 83 MHz) |

*Typical value @ 25°C; decrease possible with added cooling

# Spiden chips offer improved performance for both spectroscopy and imaging applications

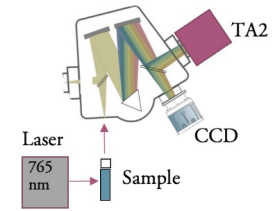
| | State-of-the-art SPAD* | Spiden ASIC | Spiden performance |
|---|---|---|---|
| **SPAD PDP @ 900nm** | < 5% | > 18% | Enhanced infrared sensitivity |
| **Temporal resolution** | > 30 ps | < 20 ps | High temporal resolution |
| **Frame rate** | 6 Hz – 97.7 kHz | 25 kHz – 1'000 kHz | High speed |
| **Applications** | 2D / 3D imaging | 2D / 3D imaging and (time-resolved) spectroscopy | Multimodality |

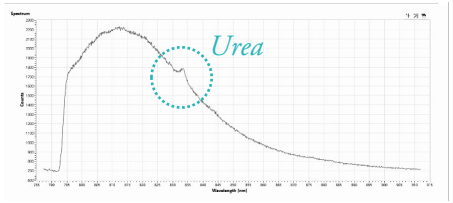
*PDP = Photon Detection Probability*
**Chips based on the same base technology as Spiden chips*

# Spiden CMOS detector technology allows for efficient fluorescence background suppression and improved SNR

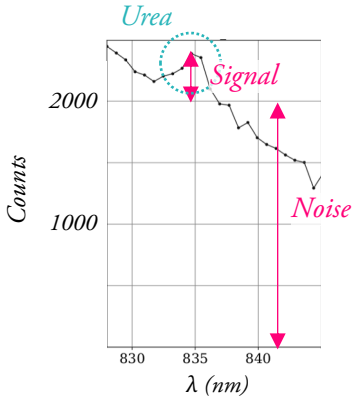
**Example setup**

*Sketch of experimental setup in Spiden laboratory*

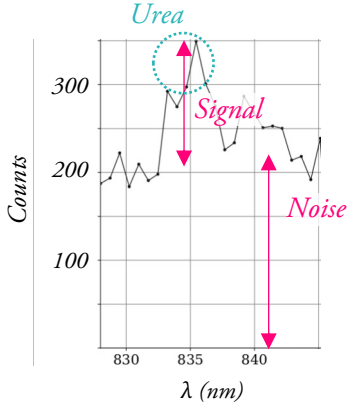



**Commercial cooled CCD**




**Spiden CMOS detector**



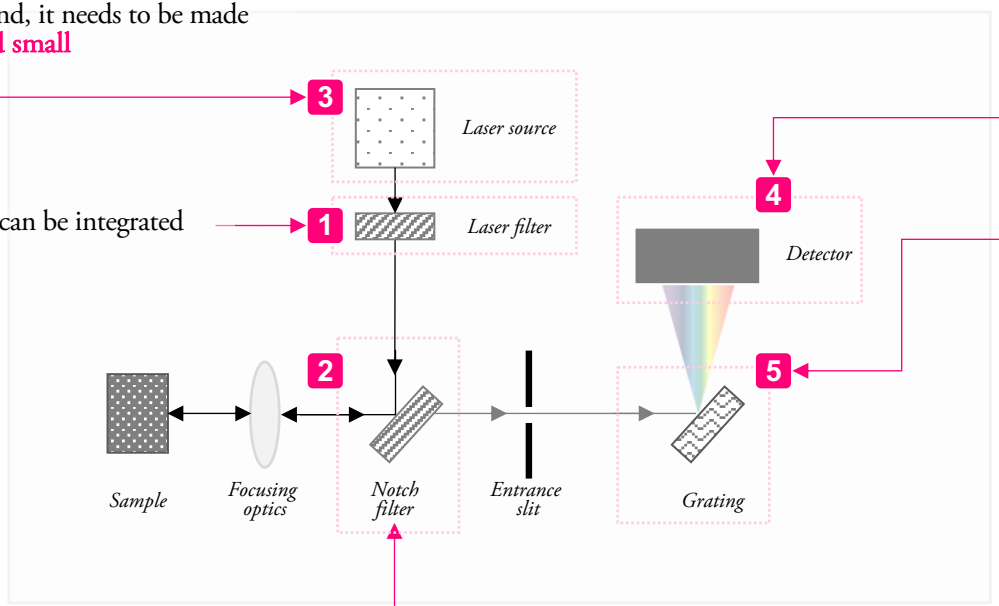

- Spiden uncooled proprietary detector was benchmarked against a scientific cooled CCD camera
- 10x reduction in fluorescence background during measurements of urea demonstrated

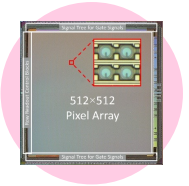
**Spiden's CMOS detector technology allows for efficient fluorescence background suppression and thus improved SNR**

# Outlook: the journey towards system-level photonic integration of spectrometers

The **laser source** can be integrated to some extend, it needs to be made **cheap and small**

Example of a Raman spectrometer

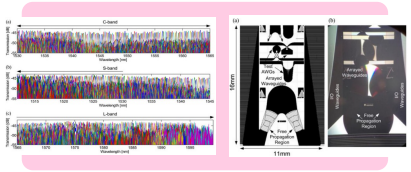



The **detector** can be integrated with CCD / CMOS / SPAD **(Charbon et al, SwissSpad2, etc.)**

The **grating** can be integrated with AWG / CMZI DWDM / interference filter:

- Need flat top-response for process & alignment tolerances
- Low-loss for low-light applications (single photons)
- Ideally coherent interference like MZI



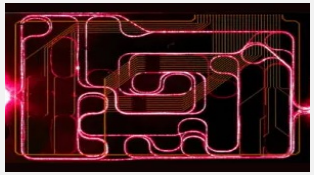
**HOWEVER: FOR INTEGRATED BIOPHOTONICS SPECTROMETERS, SOME COMPONENTS ARE STILL MISSING** *(SEE NEXT PAGE)*

# Biophotonics needs silicon nitride photonics platform and ecosystem around it (e.g., fab access, test platforms, software, people)

SPIDEN

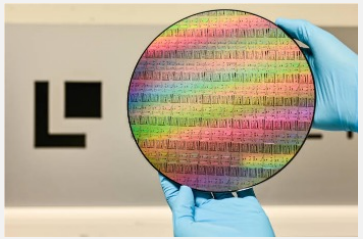
## Existing photonics platforms

### R&D and small volume



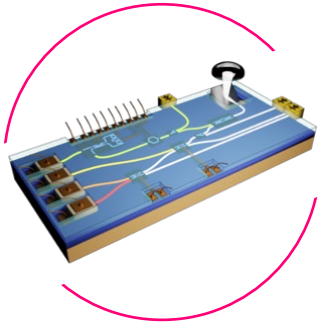
*LioniX Triplex Platform*
*IMEC BioPIX, others...*

### Large volume



*Ligentec / X-Fab*

## Spiden's product needs following currently missing building blocks



*Towards an integrated photonics spectrometer*

| | | |
|---|---|---|
| 1 | Coherent interferometers | *High photon efficiency for low light operation: every photon counts - we cannot afford reflected light!* |
| 2 | High spectral channel count per die | *Large number of channels translates to high spectrometer resolution* |
| 3 | Flat-top spectral pass bands | *Account for laser jitter, alignment tolerances and temperature drift* |
| 4 | Vertical coupling between photonics die and silicon detector chip | *High efficiency, large alignment tolerances, low divergence* |
| 5 | 850 nm single-mode photonics platform | *Water absorbs above 1400 nm, where silicon photonics works best* |

**Many components are still missing and yet to be developed**

# We built a team with deep experience in entrepreneurship, MedTech product development and Spiden's science disciplines

**Leo Grünstein**
*Founder & CEO*

**Bernd Wittner**
*Chief technology officer*

**Adler Perotte**
*Chief science & innovation officer*

**Daniel Thürig**
*VP operations & strategy*

**Övünç Okyay**
*Co-founder & venture builder*

**Fabien Rebeaud**
*Director biomedical sciences*

**Emmanuel Delamarche**
*Senior manager microfluidics*

**Mattias Cattepoel**
*Manager system engineering*

**Jens Hofrichter**
*Lead system designer optics and photonics*

**Paolo Livi**
*Team lead electronics engineering*

**J.C. Blancon**
*Team lead biophotonics*

**Jaime Moreno Mateos**
*Team lead software & machine learning engineering*

**Elizabeth Canovic**
*Lead engineer biomedical initiatives*

- Raised USD >600m (of which USD >25m for Spiden) and created 20+ ventures, of which most are successful
- Developed devices across a wide range of medical, photonic, and imaging use-cases including surgical microscope binoculars, genome sequencers, Raman spectrometers, silicon nanowire-based chemical sensor arrays, nerve-on-a-chip platforms
- Built and productionized machine learning and deep learning pipelines at scale across various industries
- Strong mix of academic, research, and industrial backgrounds including Harvard, MIT, Rice, ETH, CERN, IBM and McKinsey
- >300 papers published including many in Nature, Science, Physical Review, PLoS
- Diverse and complimentary team members from 14 countries and 5 continents

+ 30 additional full time team members across R&D, Science & Innovation and Strategy & Operations

# Things to remember from today

1. Spiden's goal is a non-invasive multi-biomarker/drug monitoring wearable for wellness as well as medical applications, and our objective is to present data proofing our transcutaneous glucose monitoring approach by H1'23 – we mainly system integrate, and only selectively invest in deep tech development such as our own light detector and our photonics engine

2. Our proprietary light detector supports time-gated Raman spectroscopy and fluorescence lifetime imaging (FLIM) at a small form factor without the need for cooling – *contact us, if you are interested*

3. Spiden is actively working towards integrated spectrometer systems using photonic integrations - the eco system needs to be developed further to meet the needs of biophotonic systems operating around 850 nm and we are open for partnering – *contact us, if you are interested*

*Contact details Jens Hofrichter*

**Questions?**

www.spiden.com